

CLAIMS

What is claimed is:

sub C4 1. An isolated and/or ~~recombinant~~ nucleotide sequence enabling a cell cycle dependent initiation of translation of mRNA.

2. The isolated and/or recombinant nucleotide sequence of claim 1 wherein said isolated or recombinant nucleotide sequence is an internal ribosomal entry site sequence.

sub a' 3. ~~The isolated and/or recombinant nucleotide sequence of claim 1 or 2 wherein said cell cycle dependency is a G2/M cell cycle dependency.~~

sub C3 4. An isolated and/or ~~recombinant~~ nucleic acid molecule encoding at least a functional part of an eukaryotic internal ribosomal entry site, which said eukaryotic internal ribosomal entry site, in a mitotic PITSLRE protein kinase gene, comprises SEQ ID NO: 1 or a functional part of SEQ ID NO: 1.

5. The isolated and/or recombinant nucleic acid molecule of claim 4 wherein said eukaryotic internal ribosomal entry site is a functional part of SEQ ID NO: 1, said functional part of SEQ ID NO: 1 comprising SEQ ID NO: 7.

6. The isolated and/or recombinant nucleic acid molecule of claim 4 further comprising at least a part of SEQ ID NO:1 or a nucleotide sequence at least substantially homologous to SEQ ID NO:1.

Sub C16

7. The isolated and/or recombinant nucleic acid molecule of claim 4, wherein said isolated and/or recombinant nucleic acid molecule comprises at least a part of SEQ ID NO:1 sufficient to encode a functional part of a eukaryotic internal ribosomal entry site, a sequence hybridizing under conventional conditions to at least a part of SEQ ID NO:1 sufficient to encode a functional part of a eukaryotic internal ribosomal entry site, or a complementary sequence of SEQ ID NO:1, said complementary sequence encoding a functional part of a eukaryotic internal ribosomal entry site.

8. An isolated and/or recombinant nucleic acid molecule selected from the group consisting of

- a) a nucleotide sequence comprising SEQ ID NO:4, SEQ ID NO:5, or SEQ ID NO:6; and
- b) a nucleotide sequence consisting essentially of SEQ ID NO:4, SEQ ID NO:5, or SEQ ID NO:6.

9. The isolated and/or recombinant nucleic acid molecule of claim 8 wherein said isolated and/or recombinant nucleic acid molecule comprises SEQ ID NO:4.

10. The isolated and/or recombinant nucleic acid molecule of claim 8 wherein said isolated and/or recombinant nucleic acid molecule comprises SEQ ID NO:5.

Sub a2

11. A chimeric gene comprising:

- a) the isolated and/or recombinant nucleotide sequence of any one of claims 1 to 10, and
- b) one or more control sequences operably linked to said isolated and/or recombinant nucleotide sequence.

12. A vector comprising the isolated and/or recombinant nucleic acid molecule of any of claims 1 to 10 or comprising a chimeric gene according to claim 11.

13. The vector of claim 12 wherein said vector is an expression vector, said vector further comprising a promoter.

sub a3 14. ~~A eukaryotic host cell comprising the nucleic acid molecule of any of claims 1 to 10 or comprising the chimeric gene of claim 11.~~

15. An expression system comprising the eukaryotic host cell of claim 14.

16. A method for cap-independent translation of mRNA in a cell, said method comprising:

introducing, into said cell, an expression vector comprising a translation control element comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:4, and both SEQ ID NO:1 and SEQ ID NO:4.

sub a4 17. ~~A method of inducing a cell cycle dependent initiation of translation in a eukaryotic cells, said method comprising introducing the isolated and/or recombinant nucleotide sequence of any of claims 1-10 into said eukaryotic cell.~~

sub a9 18. ~~The method according to claim 17 wherein the nucleotide sequence is a cell cycle dependent internal ribosomal entry site sequence.~~

19. The method according to claim 18 wherein the cell cycle dependent internal ribosomal entry site sequence is a G2/M-dependent internal ribosomal entry site sequence.

04625

20.

A pharmaceutical composition for treating and/or preventing a disease in a subject by gene therapy, said pharmaceutical composition comprising:

the vector of claim 12 or 13, or

the isolated and/or recombinant nucleotide sequence of any of claims 1 to 10 together with means for delivering said isolated and/or recombinant nucleotide sequence to the subject.

21.

A method of treating a disease in a subject, said disease selected from the group of diseases consisting of cancer, coronary artery disease, and peripheral vascular disease, said method comprising:

administering, to the subject, in a therapeutically acceptable manner, a vector, suitable for said subject in both form and amount, and comprising an internal ribosomal entry site nucleotide sequence that enables a G2/M cell cycle dependent initiation of translation of mRNA in the subject; and

thus initiating translation of mRNA in the subject.

22.

The isolated and/or recombinant nucleic acid molecule of claim 8 wherein said isolated and/or recombinant nucleic acid molecule comprises SEQ ID NO:6.

adc

'>

ADD

Db

add

F1